Health Care Provider Fact Sheet

Disease Name	**Methylmalonic acidemia, Vitamin B-12 responsive**
Alternate name(s)	Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in adenosylcobalamin, cblA complementation type; Methylmalonic acidemia, cblA type; Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in synthesis of adenosylcobalamin, cbl B complementation type
Acronym	MMA, MMAA/MMAB
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Methylmalonic acidemia, Vitamin B-12 non-responsive; Combined deficiency of methylmalonyl-CoA mutase and homocysteine
Symptom onset	Variable. Ranges from the first days of life to completely asymptomatic.
Symptoms	Episodic ketoacidosis with vomiting accompanied by lethargy and coma which can lead to death. Survivors can have developmental delays, growth retardation, spastic quadriparesis, dystonia and seizures. Neutropenia, thrombocytopenia and osteoporosis are common complications.
Natural history without treatment	Variable depending on the enzyme defect. Some will die in the newborn period, others will survive with deficits and others will be asymptomatic.
Natural history with treatment	**CblA:** Good prognosis with injections of hydroxy-cobalamin (OH-cbl) which reverses biochemical and clinical abnormalities in about 90% of patients. **CblB:** Equal fractions of affected patients are alive and well, alive and impaired, or deceased. The age of onset of symptoms can help prognosticate outcome – those patients with a later onset of symptoms have a more benign course. Approximately 40% of patients will respond with a drop in MMA level when given OH-cbl injections.
Treatment	Protein restricted diet, OH-cbl injections, carnitine supplementation, oral antibiotic therapy to decrease proprionate and medical foods. Liver transplant or combined liver/kidney transplant may increase metabolic control, but may not prevent neurologic complications.
Emergency Medical Treatment	See sheet from American College of Medical Genetics (attached) or for more information, go to website: http://www.acmg.net/StaticContent/ACT/C3.pdf
Physical phenotype	Minor facial dysmorphisms including high forehead, broad nasal bridge, epicanthal folds, long, smooth philtrum and triangular mouth. A variety of skin lesions can be seen in patients due to moniliasis.
Inheritance	Autosomal recessive
General population incidence	1:48,000
Ethnic differences	No known population at increased risk
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondria
Enzyme Function	Production of adenosylcobalamin
Missing Enzyme	Cobalamin A (cblA) deficiency: cobalamin reductase Cobalamin B (cblB) deficiency: cobalamin adenosyltransferase
Metabolite changes	Elevated glycine in urine
Prenatal testing	Possible via enzyme assay on amniocytes or CVS..
MS/MS Profile	Elevated C3 propionyl carnitine, elevated C4 DC methylmalonyl carnitine.
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=251000
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org Fatty Oxidation Disorder (FOD) Family Support Group www.fodsupport.org

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